set of recurring motion patterns. The complete set of these patterns, which we tentatively call the dynasome, spans a high-dimensional space whose axes, the dynasome descriptors, characterize different aspects of protein dynamics.
Methodology: The unique dynamic fingerprint of each protein is represented as a vector in the basis of this dynasome space. The difference between any two vectors, consequently, gives a reliable measure of dynamics similarity. From extended molecular dynamics simulations of 100 representatively chosen soluble proteins, dynamics fingerprints were obtained, which served to characterize in detail the statistical properties of the dynasome.
Conclusions: 1. We find that proteins do not fall into natural, well separated dynamics classes. 2. Four collective dynamics descriptors obtained from PCA are sufficient to characterize the dynasome. 3. For the majority of proteins we observe strong correlation between structure and dynamics. Exceptions are convergent and divergent dynamics, respectively, where minor structural differences yield major dynamics differences and vice versa. 4. Proteins with similar function carry out similar dynamics. Combination of structural and dynamics data yields superior predictions of protein function.

949-Plat
A Model Comparison for Characterizing Protein Motions from Structure
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To understand the extent structure plays in determining protein dynamics, a comparative study is made using three computational models that characterize native state dynamics starting from known protein structures taken from four distinct SCOP classifications. A geometrical simulation [1] (FRODA) is performed based on an initial rigid cluster decomposition using FIRST [2], and the results are compared to the commonly employed elastic network model (ANM) and molecular dynamics (MD) simulations. The essential dynamics is quantified by a direct analysis of a mode subspace constructed from ANM and a principal component analysis (PCA) on both the FRODA and MD trajectories using root mean square inner (RMSIP) product and principal angles (PA). Relative subspace sizes and overlaps are visualized using the projection of displacement vectors on the model modes. Additionally, a mode subspace is constructed from PCA on an exemplar set of X-ray crystal structures in order to determine similarly with respect to the generated ensembles. Our quantitative analysis reveals there is significant overlap across the three model subspaces and the model independent subspace. The subspaces generated from all three models were found to have high overlap for all four SCOP classes of proteins investigated, although FRODA provided the most robust sampling of the native basin. These results indicate that structure is the key determinant for native state dynamics. This work is supported by NIH grant 1R21HL093531.
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950-Plat
Discovering Conformational Sub-States Relevant to Protein Function
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Native protein dynamics are governed by a hierarchical energy landscape, a multi-level configurational space whose hills and valleys correspond respectively to transition states and stable conformational sub-states. Internal motions enable proteins to explore this rugged landscape; increasingly, proteins are conceptualized as richly diverse ensembles rather than static structures. But the role of conformational fluctuations (or multiple conformations) in designated function of proteins is widely debated. Recent evidence indicates that sub-states of protein conformations exist containing both structural and dynamical features important for function. The low populations in these sub-states and the transient nature of conformational transitions have presented significant challenges for their identification and characterization. To overcome this challenge we have developed quasi-anharmonic analysis (QAA). QAA utilizes higher-order statistics of protein motions allowing identification of various states in the conformational hierarchy; further, the focus on anharmonicity allows the identification of conformational transitions between sub-states. QAA of equilibrium simulations of human ubiquitin and T4 lysozyme, elucidates a hierarchy of functionally relevant sub-states and protein motions involved in molecular recognition. In combination with a reaction pathway sampling method, QAA allows characterization of conformational sub-states associated with an enzyme reaction such as the cis/trans isomerization of peptidyl-prolyl amide bonds catalyzed by the enzyme cyclophilin A. In all three cases QAA reveals presence of a number of conformational sub-states at different levels in the hierarchy, with specific sub-states containing crucial structural and dynamical elements relevant for identification of binding other proteins (ubiquitin), binding substrate (lysozyme) and enzyme-substrate interactions in the active-site for the transition state formation and reaction mechanism (cyclophilin A). Overall, QAA provides a novel framework to intuitively understand biophysical basis of conformational diversity and its relevance to protein function.

951-Plat
Conformational Dynamics and Allostery of Supramolecular Protein Assemblies: from the Nuclear Pore Complex to GroEL
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Supramolecular protein assemblies participate in a broad range of cellular functions including transcription, translation, protein synthesis and folding, translocation of biomolecules, and cell division. Single particle cryo-electron microscopy is increasingly revealing the structure of diverse high molecular weight protein assemblies at ever higher resolution. While the static structure of these assemblies provides invaluable insight into their functional mechanism, important additional information is provided by their conformational dynamics. Here we present an unsupervised computational framework that is used to analyze the conformational dynamics of the majority of structures deposited in the Electron Microscopy Data Bank. Conformational dynamics are computed using normal mode analysis based on a recently established finite element framework, which is used to compute equilibrium thermal fluctuations, elastic strain energy distributions associated with specific conformational transitions, and dynamical correlations in distant molecular domains. Results are presented in detail for the nuclear pore complex from Dictyostelium discoideum and the chaperonin GroEL from Escherichia coli, revealing regions that are important to the stability of these molecules, as well as highly coupled dynamically in collective molecular motions. Results are publically available at http://www.cdyn.org and will be extended to include proteins in the Protein Data Bank, offering an important source of dynamical information that may be used to investigate the biological function of a broad range of molecules.

PLATFORM R: Membrane Structure II

952-Plat
Charachterizing Structure and Dynamics of Calcium-Induced Clusters of Phosphatidylserine in Mixed Lipid Bilayers
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The cellular membrane plays a key role in the regulation and activation of peripheral membrane proteins. For instance, the enzymatic activity of several coagulation factors and signaling proteins is regulated by their specific binding to negatively charged regions of the cellular membrane that are rich in anionic lipids such as phosphatidylserine (PS). The lipid composition of the membrane and the ionic content of the immediate solution significantly modify structural properties of the bilayer surface. In particular, calcium-induced clustering of PS lipids has been suggested to modulate membrane-protein interactions. We employ our novel highly mobile membrane mimetic (HMMM) model combined with molecular dynamics simulations to investigate structural and dynamic properties determining these interactions. The HMMM model, while preserving full representation of the lipid head groups that are required for detailed characterization of specific interactions, provides 1-2 orders of magnitude speed up in lipid mobility. Extended simulations with HMMM systems including anionic (POPS), zwitterionic phosphatydilcholine (POPC), or POPS/POPC binary mixtures provide a detailed view of structural changes that occur due to lipid-lipid and lipid-ion interactions, specifically those that drive PS clustering. Simulations revealed a diverse set of PC-PS-Ca2+ microdomains of consistent geometry. In particular, we observed 2PC:2PS:Ca2+:water and 2PS:Ca2+:3water stoichiometries. Ca2+ ions interact with phosphate groups of PC and PS as well as with the carboxy groups of PS. Interestingly, unimolecular chelation of Ca2+ by the same PS head group is often observed within the clusters. In contrast to monovalent Na+, the presence of divalent Ca2+ shows its long-lived coordination with lipid head groups that modulates their orientation and leads to formation of PS clusters. Prior to the development of the HMMM method these observations were out of reach of atomistic simulations.